DRAFT

SUMMARY POSITIONS

CONSTITUENTS OF TOBACCO SMOKE

1. The chemical constituents present in tobacco smoke are the same as those found in many other products.

2. No constituent, at levels found in tobacco smoke, has been scientifically proven to cause cancer, or any other disease, in humans.

3. There are many other sources of chemical constituents of tobacco smoke.

4. Cigarette packs in Australia are already comprehensively labelled.

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THE CHEMICAL CONSTITUENTS PRESENT IN TOBACCO SMOKE ARE THE SAME AS THOSE FOUND IN MANY OTHER PRODUCTS AND FROM MANY OTHER SOURCES

At least 3800 chemical compounds have been identified in tobacco smoke. Ninety percent of cigarette smoke is air, water and carbon dioxide, a natural by-product of combustion. Of the remaining ten percent, only a few substances such as nicotine and carbon monoxide (CO) are detectable at levels above one milligram per cigarette. The vast majority of the remaining compounds in cigarette smoke are present only in extremely small amounts, measured in micrograms (ug) (millionths of a gram) or nanograms (ng) (billionths of a gram) per cigarette. Although under experimental conditions involving laboratory animals and high concentrations, some substances in cigarette smoke can have a toxic or disease-inducing effect, the concentrations at which a smoker is exposed to these substances have not been determined to have any health effects on humans. Although tobacco smoke constituents are among the most heavily researched substances in the world, no constituent at levels found in cigarette smoke has been scientifically proven to cause cancer or any other disease in humans.

Most chemicals found in tobacco smoke are also present in our indoor and outdoor environments, the food we eat, and the water we drink. It is therefore misleading and scientifically irresponsible to suggest that there is something "unique", and hence hazardous, about the presence of these substances in cigarette smoke.

Food is a source of chemicals in the following ways:

* 'natural' chemicals already present in food eg formaldehyde in fruits and vegetables;

* chemicals added during production or growing of food eg agricultural chemicals, fertilizers and environmental contamination;

* chemicals added during the processing of food;

* chemicals added during the packaging and storage.

Many of the ordinarily occurring chemicals in food are the same chemicals that are present in tobacco smoke. Cooking food also generates a variety of chemicals that have been claimed to cause cancer eg nitrosamines from cooking bacon, and benzpyrene from barbecued meat.

NO CONSTITUENT, AT LEVELS FOUND IN TOBACCO SMOKE, HAS BEEN SCIENTIFICALLY PROVEN TO CAUSE CANCER, OR ANY OTHER DISEASE IN HUMANS

Frequently, anti-smoking organisations claim that there are around 43 known carcinogens in tobacco smoke. This claim is based on an analysis of information pertaining to the claimed cancer-causing properties of tobacco smoke constituents carried out by the International Agency for Research on Cancer (IARC) in 1986. This list was also adopted by the US Surgeon-General in 1989. There are several points that have to be made relating to this claim:

* It is generally accepted by toxicologists that <u>any</u> chemical substance is toxic to humans if the level of exposure is high enough and <u>no</u> substance is toxic if the level of exposure is low enough. For example, arsenic in small quantities has been used for medicinal purposes; in high concentrations, however, it is well known that arsenic is poisonous to humans. The amount of almost all individual constituents of cigarette smoke are extremely low, measured in millionths (micrograms) and billionths

(nanograms) of a gram. Similarly, the fact that high doses of a chemical may cause tumours does not necessarily mean that small doses will. The body is well-equipped to deal with low doses of chemicals since people are continually exposed to them in everyday life.

It is frequently stated, in this regard, that over a period of many years, cigarette smokers are in fact exposed to large amounts of these chemical constituents. However, this is no different from cumulative exposure to the same chemicals (usually at higher doses) from food, water or breathing air over a lifetime.

* Many of the 43 chemicals usually claimed to be carcinogens are so claimed based only on information in animals, and not in humans. Positive results (ie tumours) in animal tests are usually based upon unrealistically high doses (so called "maximum tolerance doses") of the compound in question, and the compounds are frequently administered in ways that bear no relevance to the human smoking situation eg administration by mouth, by injection, or painting onto the skin of animals. There are several other problems in interpreting the results of animal studies eg there is increasing awareness among scientists that misleading positive results are frequently reported because of inappropriate design of tests (for example, cases of tumours called sarcomas, at the site of injection of a number of substances, are generally not considered to be evidence of carcinogenity). The claimed tumour may be an artefact arising from irritation caused by an unrealistically high dose of the chemical being tested, or it may arise from an unrealistic feeding regime commonly employed in animal studies. It is known that the usual practice

of providing test animals with unlimited food increases the number of observed tumours.

* In addition to these problems of interpreting the results of animal studies it should be noted that many regulatory authorities have recognised that interpretation of findings with individual chemicals in relation to complex mixtures such as tobacco smoke is difficult if not impossible. For example, experiments that have exposed animals even to high levels of whole tobacco smoke by the appropriate method of administration (inhalation) have not generally confirmed that there is a carcinogenic effect.

* OTHER SOURCES OF SOME CHEMICAL CONSTITUENTS OF TOBACCO SMOKE

As discussed above, a number of substances in tobacco have been claimed to be carcinogens (1) and have been listed in a US Surgeon General's report on smoking and health issues (2).

Discussions of some of the constituents found in tobacco smoke, listed by the Surgeon General (2), follows.

It should be noted that the Surgeon General's figures are for plain (ie non-filter) cigarettes and do not take account of filtration and the lower yield of modern commercial cigarettes. His figures are therefore very much on the high side for typical cigarettes of today.

The following considers other sources of some of these substances under sub-headings as used in the Surgeon General's listing:

Polycyclic aromatic hydrocarbons (PAH)
Aza-arenes

N-nitrosamines
Aromatic amines
Aldehydes
Miscellaneous organic compounds
Inorganic compounds

Polycyclic Aromatic Hydrocarbons (PAH)

The Surgeon General's report cites only benzo(a)pyrene (BP) as present in processed tobacco though other PAH are present in cigarette smoke. BP is present in mainstream smoke (per non-filter cigarette) at a level of 20-40 ng. BP occurs ubiquitously in products of incomplete combustion (3). It also occurs in fossil fuels (3). It has been found at 0.05 - 74 ng/m^3 in urban air; at 50-81 ug/litre fuel in gasoline engine exhaust; at 8 ug/kg in charcoal-broiled steaks; at 0.1-16.5 ug/kg in roasted coffee and up to 48.1 ug/kg in fruit, vegetables and cereals (3). Researchers recently concluded that the amount of BP in a single char-grilled steak was equivalent to that in the smoke from 600 cigarettes (4). It is also present when fish is broiled or smoked. It is a common contaminant of air, water, and food; and is a constituent of most types of smoke (5).

AZA-ARENES

Dibenzacridine

Dibenzacridine has been reported to occur in two forms in mainstream cigarette smoke: dibenz(a,h)acridine (0.1ng per cigarette) and dibenz(a,j)acridine (3-10 ng per non-filter cigarette) (2). It is formed from incomplete combustion of organic materials eg refuse burning, motor vehicle exhausts, industrial processes. It is commonly present, therefore, in urban air (0.1 ug/1000 m^3)(6a).

NITROSAMINES

The Surgeon General (2) lists 7 nitrosamines present in tobacco. Nitrosamines are formed from compounds such as nitrates and nitrites, together with other naturally occuring compounds known as secondary amines. Nitrates and nitrites are common constituents of foods, especially vegetables, and are also used as food additives. Secondary amines are widespread in foods; fish and cheese having particularly large amounts.

Hoffmann et al (6) tested food (mainly dairy products) and food containers for N-nitrosomorpholine (NMOR). Levels ranged from "not detected" to 3.3 ng/g in a French semi-soft cheese. It was concluded that this was formed by nitrosation of morpholine which had diffused from container waxes to the food. Thus NMOR can occur in products, including tobacco, if they are wrapped in materials containing morpholine. The amount of NMOR generated is likely to depend, other things being equal, on the amount of morpholine and nitrosating agent, such as nitrite, present. Another Hoffmann paper (7) noted that the precursor morpholine is not known to naturally occur in tobacco.

Nitrosomorpholine has been patented as a solvent for polyacrylonitrile and as a chemical intermediate in the synthesis of N-aminomorpholine. It has also been found to be effective against microbial infections. No evidence of its commercial use for these purposes has been found (8). Therefore, the only likely source of exposure is as described in the previous paragraph. Data on levels of NMOR in mainstream smoke are not available (2).

The presence of N-nitrosodimethylamine (DMNA) has been reported in mainstream cigarette smoke at levels around 25 ng per cigarette (2). DMNA is also found in beers and whiskies (9); and in meat and fish products, as demonstrated in a number of studies at levels up to 80 ng/g in Canadian meat

products in 1972 and in USA frankfurters (also in 1972) (8). Bacon can be a significant source of DMNA and N-nitrosopyrrolidine (NPYR) because of added nitrite. In a Canadian study (10) cooked bacon contained 2-18 ng/g DMNA and 18-121 ng/g NPYR. The fumes contained 2-49 ng DMNA and 8-204 ng NPYR, calculated per gram of bacon. NPYR has been found in other food products based on a number of studies, but at levels lower than found in bacon (8). NPYR is present in mainstream cigarette smoke at levels of 1.5-110 ng per non-filter cigarette (2).

N-nitrosodiethanolamine (NDELA) was found in all of 7 facial cosmetic formulations at levels of 42-49 ng/g, in 12 of 13 hand and body lotions (<10-140 ng/g) and in 8 of 9 hair shampoos (<10-260 ng/g) (8). It has been found in cutting fluids used to reduce the temperature of metal-tool interfaces. A nitrite-triethanolamine based cutting fluid did not contain NDELA when fresh but the level increased to 400-800 mg/litre on standing 5-7 months (8). In another study, all cutting fluids examined contained NDELA at concentrations varying from 0.02-3% (8). An atrazine based pesticide emulsified with triethanolamine was found to contain 500 ng/g NDELA (8). NDELA is present in mainstream cigarette smoke at levels of 36 ng per non-filter cigarette (2).

AROMATIC AMINES

2-Naphthylamine

2-Naphthylamine is used as a chemical intermediate in the dye and pigment industry and is released onto waste water from this source. It is also a product of combustion of nitrogen-containing organic matter and is emitted to the air in this process eg coal, furnaces, etc. It degrades rapidly in the atmosphere. 2-Naphthylamine is present in mainstream cigarette smoke at a level of 1-22 ng per non-filter cigarette (2).

ALDEHYDES

Formaldehyde

Formaldehyde has been reported to be present in mainstream cigarette smoke at levels of 70-100 ug per non-filter cigarette.

Formaldehyde data have been taken from an IARC monograph (11). 2710 million kg were produced in the USA in 1979. This was reported in terms of a 37% aqueous solution "formalin" even though a variety of forms was produced. Formaldehyde is also produced in Canada, Western Europe, Japan, Central and Southern America, Eastern Europe, Australia, Africa and Asia (in addition to Japan). The US use-pattern for formaldehyde in 1978 is estimated to be: 60% plastics and resins; 22% production of intermediates and 18% miscellaneous. Urea-formaldehyde resins accounted for 25% of total US production. These are used as adhesives in particleboard, fibreboard and plywood. Another application is in insulation foams.

Formaldehyde occurs in air as a product of natural photo-oxidation of atmospheric hydrocarbons emitted from automobile exhausts. Levels in automobile exhaust itself have been measured at 36-53 mg/m^3. Formaldehyde may occur in indoor air as an emission from urea-formaldehyde foam insulation or from particleboard. In Danish homes containing particleboard, levels in the range 0.08-2.24 mg/m^3 have been found.

In a US study, levels in the range 0.01-39 mg/m^3 were found where urea-formaldehyde foam was implicated. Formaldehyde may be present in foods either naturally or by contamination. A Japanese study found levels up to 17 ug/g in various fruits and vegetables. Formaldehyde occurs in fingernail hardeners. It is also used extensively in pathology and by undertakers.

Acetaldehyde

Acetaldehyde is present in mainstream cigarette smoke at levels of 18-1400 ug per non-filter cigarette (2). Acetaldehyde data have been taken from another IARC monograph (12). US production is less than for formaldehyde and peaked in 1969 at 748 million kg.

It is used primarily as a chemical intermediate, mainly for acetic acid. A survey of US industry reported 8,600 kg used in 1976 as a component of many flavours added to a variety of foods, eg apples, broccoli, coffee, citrus and other fruits etc. It is a product of alcohol fermentation and has been found in beer (2.6-13.5 mg/litre) and wine (0.2-1.2 mg/litre). It is a combustion product of wood, with one estimate of 0.7 ug/g and diesel exhaust (0.05-6.4 mg/m^3).

Crotonaldehyde

Crotonaldehyde is present in mainstream cigarette smoke at levels of 10-20 ug per non-filter cigarette (2). Crotonaldehyde production in the USA in 1977 was 500 thousand kg, suggesting substantially less opportunity for industrial exposure than for the other two aldehydes. Its main use is as an intermediate in the production of other chemicals. It is also used as a solvent in purification of mineral oils, manufacture of resins and rubber antioxidants. Data on crotonaldehyde levels in the environment have been difficult to find, partly because measurements are often made as "aldehydes" or "total aldehydes". Crotonaldehyde has been detected in strawberries (13). It has been detected in gasoline exhausts (0.3-4 mg/m^3) (14). Fossil-fuelled power stations emit aldehydes (13) but specific aldehydes, apart from formaldehyde are not specified. In summary it may be assumed that the main source of crotonaldehyde in the environment is from the combustion of a variety of natural organic substances.

MISCELLANEOUS ORGANIC COMPOUNDS

1-Dimethylhydrazine

No data are available (2) regarding levels of 1-dimethylhydrazine in mainstream cigarette smoke, although it is present in processed tobacco at 60-147 ug per gram. It has been determined in various fruits, including cherries (15a), apples (15a,b) and peaches (15b). It has been suggested that its presence in tobacco might arise from bacterial or enzymic processes occurring during curing (16).

Ethyl Carbamate (Urethane)

Ethyl carbamate is present in mainstream cigarette smoke at levels of 20-38 ng per non-filter cigarette (2). Sax (4) comments as follows. It has been found in over 1000 beverages sold in the USA. The major liquor sources are bourbons, sherries and fruit brandies (some had 1000 to 12,000 ppb). Many whiskies, table and desert wines, brandies and liqueurs contain high amounts. It is formed as a natural by-product of fermentation. It is also found in cheese, yogurt and soy sauce (17). A limit of 125 ppb in alcoholic beverages was to be introduced in the USA in 1989.

Vinyl Chloride

Vinyl chloride is present in mainstream cigarette smoke at levels of 1-16 ng per non-filter cigarette (2). Vinyl chloride is a gas that is detectable in various food products such as honey, butter, ketchup and syrup. It is also present in some wines (18). Vinyl chloride is also used in the manufacture of plastics (19). A recent literature reviewer concluded that vinyl chloride is present in cigarette smoke "apparently at levels too low to be considered a carcinogen or fibrosis-inducing agent" (20).

INORGANIC COMPOUNDS

Hydrazine

Hydrazine is present in mainstream cigarette smoke at levels of 24-43 ng per non-filter cigarette (2). An IARC Monograph (20a) comments as follows. Hydrazine has been found to be a primary product of nitrogen fixation by Azotobacter agile. The use of hydrazine in boiler water treatment might result in its brief appearance in waste discharge, but it would react rapidly with oxygen. The use of hydrazine as a chemical intermediate would not be likely to result in its appearance in unreacted form in the environment.

Hydrazine is very reactive in a number of situations (5) and it should be concluded that it is not present in most environments. However, hydrazine is present in edible mushrooms.

Arsenic, Nickel, Chromium, Cadmium and Lead

Discussion of other sources of these substances is mainly restricted to food levels, and is based on a 1972 review (22). A more recent IARC publication (23) has also been consulted. These "trace elements" occur in all foods as natural or inherent components of plants and animals. They may also be present as a result of accidental contamination or of deliberate addition. Accidental contamination of food crops arises from, for example, atmospheric pollution. Deliberate addition to foods may occur to improve nutritive value, or they may also be added indirectly through their presence in preservatives etc.

It is estimated that less than one percent of these compounds in tobacco is transferred to the smoke, with the remainder left in the ash.

Arsenic

Levels of arsenic in mainstream cigarette smoke have been reported at 40-120 ng per non-filter cigarette(2). A typical US adult diet was estimated in 1966 to supply 0.9 mg arsenic per day, giving an overall concentration of about 1 ug/g on a dry basis. Foods of marine origin are much higher in arsenic - mussels, shrimps and prawns being in the range 42-174 ug/g.

Nickel

Levels of nickel in mainstream cigarette smoke have been reported at 0-600 ng per non-filter cigarette(2). A US adult diet has been estimated to supply 0.3-0.6 mg nickel per day, or 0.4-0.8 ug/g on a dry basis. There is some evidence that tea (7.6 ug/g) and oysters (6 ug/g dry) are exceptionally rich in nickel. Green leafy vegetables are also high in nickel (up to 3.5 ug/g).

Chromium

Levels of chromium in mainstream cigarette smoke have been reported at 4-70 ng per non-filter cigarette(2) Chromium concentrations in vegetable tissues have been reported in the range 0.01 to 1 ug/g, with levels in most foods of plant origin lying between 0.1 and 0.5 ug/g. Reported dietary intakes are variable ranging from 50-400 ug per day.

Cadmium

Levels of cadmium are present in mainstream cigarette smoke at 41-62 ng per non-filter cigarette(2). Oysters are relatively rich in cadmium (3-4 ug/g) compared with levels one tenth or one hundredth in most other foods. Cadmium is also found in other food and dairy products. Cadmium may also be obtained from air and water supplies. Soft water left overnight in galvanized or black polythene pipes can take up 0.15-1.1 ug per litre. Cadmium level in the air of 28 US cities was in a range from undetectable to 0.06 ug/m^3. In the USA, dietary

cadmium intakes by children have been estimated at 0.032-0.158 mg/day.

Lead

The Surgeon General did not report levels of lead in mainstream cigarette smoke (2) but it occurs at 8-10 ug per gram in processed tobacco. Average intakes from food by adults have been estimated in the range 0.22-0.4 mg per day. This approximates to 0.3-0.5 ug/ dry diet. Lead is present in air, soil and water.

Polonium-210

The level of polonium-210 in mainstream cigarette smoke quoted in the Surgeon General's report (2) is expressed in units of picocuries (pCi) and is reported to be 0.03-1.0 pCi per non-filter cigarette. Data are available on the total alpha-particle activity of foods (22). Values vary from less than 0.001 to 17 pCi/g. It has been estimated that an adequate Western diet is not likely to contain less than 2-5 pCi of alpha-activity per day. In general, values are low for milk products, fruits and vegetables but high for cereals and nuts.

With regard to polonium-210, a study in the area of Rostov-on-the-Don, USSR, (24) found the main route of intake in the human body is ingestion with foodstuffs. Levels in plant foodstuffs ranged from 0.0009 pCi/g (wet) for tomatoes to 0.005 pCi/g for barley. Meat averaged 0.003 pCi/g and bream fish contained a higher level, 0.012 pCi/g. Drinking water from different sources averaged 0.048 pCi/litre. Ground-level air concentrations averaged 3.6×10^{-3} pCi/m^3 over 3 months. This study was conducted in the early 1970s. On the basis of the food results it was estimated that mean daily intake by an adult was 4 pCi of polonium-210. This paper also notes that atmospheric fallout is the main source of this substance in vegetable foodstuffs. Researchers have discounted the claimed

risk to smokers of inhaled polonium-210, noting the extraordinarily minute quantities at which it is present (12).

Miscellaneous Substances

Acetone

Acetone is present in mainstream cigarette smoke at level of 100-250 ug per non-filter cigarette (22a). Acetone is most commonly encountered either at work or at home in the form of cleaning solvent. It has also been detected in freeze-dried foods and dried mil. Moreover, acetone is a naturally occurring constituent of human blood and urine (26).

Acetone is not considered toxic at low levels of exposure.

Ammonia

Ammonia is present in mainstream cigarette smoke at levels of 50-130 ug per non-filter cigarette (22a). Ammonia occurs naturally as a part of protein metabolism in man and in virtually all species of animals. Ammonia is widely used as a fertilizer. It is also a common household cleanser (27).

One researcher recently noted that:

> "The biologic significance of inhaled ammonia in the concentrations generated in mainstream smoke, which are very low, is purely conjectural "(28).

Butane

Butane is present in mainstream cigarette smoke at levels of 56-95 ug per cigarette (22b).

Butane occurs in natural gas and is present in the atmosphere as the result of the combustion of gasoline and other

petroleum products. Butane is also frequently used as an aerosol propellant. The inhalation of butane has not been demonstrated to have chronic health effects in humans (29).

Hydrogen Cyanide

Hydrogen cyanide (HCN) is present in mainstream cigarette smoke at levels of 400-500 ug per non-filter cigarette (22a). Hydrogen cyanide (HCN) is also generated by the combustion of carbon materials in air, for example, during home cooking. HCN is used in a variety of industrial processes and is also present in such varied food products as bitter almonds, lima beans, soybeans, apricots, cassava and linseed. It has been detected in certain wines (30).

A reviewer concluded that the effect of HCN in cigarette smoke, if any, on humans "remains to be determined" (31).

Methanol

Methanol is present in mainstream cigarette smoke at levels of 90-180 ug per non-filter cigarette (22a). Methanol is used in enamels, dyes, stains, cleaning solvents, paint and varnish removers, anti-freeze mixtures, and as fuel for internal combustion engines. It is also present in bread, soy sauce and various fruits and vegetables (32).

Methanol can be a skin and eye irritant in large concentrations. One researcher recently noted, however, that "considering the dose of methanol estimated to be toxic to humans (1 g/kg), it is unlikely that a normal human being could ever be exposed to enough of it by inhalation to experience acute toxicity" (33).

Napthalene

Napthalene is present in mainstream cigarette smoke at levels of 2-3 ug per cigarette (22c). It is used extensively in the

chemical, plastics and dye industries. In the home, it is found frequently in air fresheners, moth balls, varnishes and wood preservatives. Radishes also contain napthalene.

Toluene

Toluene is present in mainstream cigarette smoke at levels of 160 ug per non-filter cigarette (22a). Toluene is present in the atmosphere as a result of industrial emissions, automobile emissions, and gasoline evaporation. Exposures at home include inks, dyes, and perfumes (34). At low levels and concentrations, toluene has not been found to be toxic or to cause chronic disease in humans (35).

Phenol

Phenol is present in mainstream cigarette smoke at levels of 60-140 ug per non-filter cigarette (22a). Phenol has a variety of industrial uses, including the manufacture of perfumes, plastics and fertilizers. Phenol occurs naturally in animal tissues; the consumption of meat has been identified as the primary source of human exposure to phenol. It is also present in tap water (36). One reviewer of the literature concluded "there is no specific evidence of human cancer attributable to phenol or related compounds" (37). A researcher likewise reported that phenol is not present in cigarette smoke at high enough concentrations to have any demonstrated health effects on smokers (38).

Pyrene

Pyrene has been reported to be present in mainstream cigarette smoke at 0.017-0.14 ug per cigarette (39).

Pyrene's release to the environment is ubiquitous since it is a product of incomplete combustion eg motor vehicle and engine exhausts, stoves and furnaces, industrial processes, etc. It has been found in urban air at levels of 0.08-36 ng/m^3 (40).

It, like other polycyclic aromatic hydrocarbons, is found in cooked foods, especially char-broiled (39). It is found in smoked meats, fish and cheese at levels of 0.5-11.2 ppb and in unsmoked cheese and fish at levels of 0.7-1.4 ppb (41). Pyrene is also present in fruit and sugar, root vegetables, beverages, vegetable oils, yeast, cereals and the total UK dietary intake has been estimated at 0.016 mg/kg/day (42).

Pyrene has also been reported in drinking water at concentrations of 0.30-12 ng/litre (43).

CIGARETTE PACKS IN AUSTRALIA ARE ALREADY COMPREHENSIVELY LABELLED

Under an existing voluntary agreement between the Industry and the Federal Department of Community Services & Health, cigarette packets in Australia are labelled with levels of 'tar' (corrected particulate matter), nicotine, and carbon monoxide.

Many of the constituents of cigarette smoke are present in particulate matter and they do not differ in identity between brands. Adding information about the amounts of individual constituents, brand for brand, does not therefore contribute significantly to the consumer's ability to make an informed choice about which brand of cigarettes he or she should smoke. Provision of a long list of chemicals (virtually all of which would be unrecognisable to the consumer) would only serve to confuse consumers and would not provide the context of their much greater exposure to these same chemicals from other sources such as food, water and air.

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